201-14643

NCIC HPV
Sent by: Mary-Beth Weaver

08/05/2003 12:24 PM

To: NCIC HPV, moran.matthew@epa.gov
cc:
cc:
Subject: Response to EPA Comments - GE Plastics CAS RNs 550-44-7, 41663-84-7, 527-60-6

"John P. Van Miller" <jvanmiller@toxregserv.com> on 08/05/2003 10:49:18 AM

To: oppt.ncic@epamail.epa.gov, Rtk Chem/DC/USEPA/US@EPA
cc: "Ronald L Joiner (GEP)" <Ronald.Joiner@gepex.ge.com>, Stephen Dimond <stephen.dimond@gep.ge.com>

Subject: Response to EPA Comments - GE Plastics CAS RNs 550-44-7, 41663-84-7, 527-60-6

Attached please find responses to EPA's comments on the following Test Plans for the HPV Chemical Challenge Program:

1) N-Methylphthalimide (PI: CAS RN 550-44-7)
2) 4-Nitro-N-Methylphthalimide (4-NPI: CAS RN 41663-84-7)
3) 2,4,6-Trimethylphenol (246-TMP: CAS RN 527-60-6)

Thank you.

John P. Van Miller, Ph.D., DABT
Toxicology/Regulatory Services
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PI_CAS 550-44-7_GE Response_August 5 2003.pdf

4-NPI_CAS 41663-84-7_GE Response_August 5 2003.pdf

246-TMP_CAS 527-60-6_GE Response_August 5 2003.pdf

TRS
TOXICOLOGY/REGULATORY SERVICES, INC.

August 5, 2003

Linda Fisher, Acting Administrator
US Environmental Protection Agency
PO Box 1473
Merrifield, VA 22116

Via Electronic Submission

Attention: Chemical Right-to-Know Program, AR-201

Re: Response to Comments on Test Plan for CAS RN 550-44-7

On behalf of General Electric Company – Plastics (GE Plastics; Registration Number 1100342), Toxicology/Regulatory Services (TRS) is submitting responses to the EPA Comments on Test Plans/Robust Summaries for N-Methylphthalimide (CAS RN 550-44-7). Please address any further correspondence to:

Dr. Ronald L. Joiner
Manager, Global Toxicology
General Electric Company
One Plastics Avenue
Pittsfield, MA 01201
Phone: 413-448-6323; Fax: 413-448-6590
EMAIL: Ronald.Joiner@GEP.GE.COM

Thank you,

John P. Van Miller, Ph.D., DABT

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General Electric Company – Plastics: Response to Comments on the Test Plan for N-Methylphthalimide (CAS RN 550-44-7)

Below is a reproduction of the comments submitted to the General Electric Company – Plastics (GE Plastics) Test Plan submission for the above referenced chemical in the HPV Challenge Program. Questions and comments from EPA that require input are formatted in ***Bold/Italic*** font and GE Plastic's response follows each entry. Responses are made to specific comments rather than Summary Comments.

EPA Comments on Chemical RTK HPV Challenge Submission: N-Methylphthalimide

Summary of EPA Comments

The sponsor, General Electric Company-Plastic, submitted a test plan and robust summaries to EPA for N-methylphthalimide (CAS No. 550-44-7) dated December 30, 2002. EPA posted the submission on the ChemRTK HPV Challenge Web site on January 30, 2003.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical Properties. The data provided by the submitter are adequate for the purposes of the HPV Challenge Program. The submitter needs to enter the correct value (1.29) for Log Pow in its robust summary.

2. Environmental Fate. The data provided by the submitter are adequate for the purposes of the HPV Challenge Program. The submitter needs to address some deficiencies in the photodegradation robust summary.

3. Health Effects. Available data were adequate for acute toxicity, repeated-dose and genetic toxicity endpoints for the purposes of the HPV Challenge Program. EPA agrees with the submitter's approach to do a combined screening test for reproduction and developmental endpoints.

4. Ecological Effects. Data submitted for all ecological endpoints are adequate for the purposes of the HPV SIDS-level Challenge Program.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the N-methylphthalimide Challenge Submission

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility).

The data provided by the submitter are adequate for the purposes of the HPV Challenge Program.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

The data provided by the submitter are adequate for the purposes of the HPV Challenge Program.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

For the purposes of the HPV Challenge Program, data are adequate for acute toxicity, repeated-dose and genetic toxicity endpoints. Available information does not adequately address the developmental and reproduction toxicity endpoints. EPA agrees with the submitter's proposal that testing is needed for these endpoints and recommends a combined screening test following OECD TG 421.

RESPONSE: The original proposal (see page 4 of the Test Plan) was to conduct an OECD 422 (not 421) study. The approach to all reporting/testing programs is designed to be consistent with GE's global business goals rather than to respond within a specific regulatory framework. This approach helps ensure there is no unnecessary duplication or unwarranted animal testing. The conduct of an OECD 422 study is consistent with GE's global needs and the final report is in preparation. It will be addressed in the final submission.

Ecological Effects (fish, invertebrates, and algae).

Adequate data are available for all endpoints for the purposes of the HPV Challenge Program.

Specific Comments on the Robust Summaries

Physicochemical Properties

Octanol/water partition coefficient. In section 4.0 of the robust summaries, the submitter entered the value 19 ± 2 in the first cell, corresponding to Log Pow. The submitter needs to correct this error. The correct value should be 1.29, as the submitter indicates on page 9.

RESPONSE: The value will be corrected in the final submission.

Environmental Fate and Transport

Photodegradation. In the photodegradation robust summary, the submitter included language not pertinent to this endpoint. The submitter needs to remove the paragraphs related to "*Estimation of Environmental Distributions*", "*Common Features of the Models*", and "*Model Results*". These three sections are already covered under Section 8.2-Theoretical Distribution (fugacity calculation). Section 8.2 should be changed to Section 8.1.

RESPONSE: The Photodegradation Expert Statement relates to the ECOSAR/EPIWIN model determinations. The entire text of the Expert Statement was included to ensure clarity of approach to the modeling. In the final submission, we will delete non-critical information for the model Expert Statement to comply with the EPA's request.

Health Effects

General. The substance purity was not always reported in the summaries.

RESPONSE: In all cases, each summary indicates a purity or that the purity was "not provided" in the study report. Information provided by GE Plastics indicates that the purity of PI is consistently > 99% and usually ~ 99.9%. Thus, we believe that the studies were conducted with a highly pure test material.

Developmental. There is an error on page 42. The value of 1607 for the control group entry for the "% of litters with anomalous fetuses" should be corrected.

RESPONSE: The value will be corrected in the final submission.

Ecological Effects

Invertebrates. The robust summary did not indicate the number of organisms tested at each concentration.

RESPONSE: The information will be included in the final submission.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.